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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,370	01/23/2001	Jeffrey Browning	BGN-A054RCE2	2716
959 7590 06/11/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER YAEN, CHRISTOPHER H	
			ART UNIT 1643	PAPER NUMBER
			MAIL DATE 06/11/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/767,370	Applicant(s) BROWNING ET AL	
	Examiner Christopher H. Yaen	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,11,16,26,28,29 and 37-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8,11,16,26,28,29 and 37-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/27/06, 8/24/06, 2/3/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Re: Browning *et al*

The amendment filed 3/19/2007 is acknowledged and entered into the record. Accordingly, claims 1-7,9,12-15,17-25,27, and 30-36 are canceled without prejudice or disclaimer.

Claims 8,10-11,16,26,28-29, and 37-51 are pending and examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 8,10-11,16,26,28-29,37-42,44-47, and 49 under 35 USC § 112, 1st paragraph is maintained for the reasons of record. Applicant argues that the instant specification supports the limitation of "at least 70% biologically active". Applicants contend that the support for the claimed limitation can be found in figure 9 of the drawings, in which the figure shows "about 30% dead, i.e. inactive, hLTbR at an incubation temperature of about 35 degrees C". Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Those of skill in the art may show support for claimed limitations by using descriptive means such as words, structures, figures, diagrams, and formulas that fully

set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961,1966 (Fed. Cir. 1997). In the instant case, the figure or diagram relied upon does not “fully set forth the claimed invention.” The graph shows standard deviations of +/- 2-4 percentage points and the claimed limitation of 70% is not clearly or adequately distinguished in the graph such that one of skill in the art would readily recognize that 30% was inactive. Those of skill would find the determination of at least 70% an arbitrarily designation determined from the figure. Therefore, the rejection of the claim is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 102

The rejection of claims 16 and 41 under 35 USC § 102(b) as being anticipated by Delgi-Esposti *et al* is maintained for the reasons of record. Applicant argues that the cited reference does not anticipate the claimed invention. Specifically applicant argues that the cited reference fails to teach a pharmaceutical preparation obtained from culturing cells at a reduced temperature to obtain a composition comprising 70% biologically active LTbR-Ig-fusion protein and a pharmaceutical carrier. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

As indicated in the previous office action, the phrase “biologically active” has not been adequately defined in the specification as filed. As such, the term has been interpreted to mean a composition capable of eliciting an immunological response. In this case, the reference teaches a composition purified and resuspended in PBS and

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used to immunize mice for the production of monoclonal antibodies. Moreover, as the specification as indicated, use of column chromatography methods can be used to purify "active" proteins, thereby separating the fusion protein from "inactive" proteins and producing a composition which at least 70% active protein. The methods as provided by Delgi-Esposti *et al* used mammalian cells therefore the structure of the products are deemed to be the same, in the absence of evidence to the contrary. Whether or not additional purification steps are recited in the reference is not germane to the issue at hand because the claims are constructed as product-by-process. Therefore, in the absence of some objective evidence to indicate that the method of Delgi-Esposti *et al* produces a structurally distinct product, the claims are drawn to a product per se.

Therefore the claims are maintained for the reasons of record.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 8,10-11,16,26,28-29, and 37-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ashkenazi *et al* as evidenced by *Invitrogen* Life Technologies (Baculodirect Baculovirus Expression System, 2004) or Delgi-Esposti *et al.* in view of Kaufmann *et al* (Biotechnology and Bioengineering; 1999; 63(5):573-582).

- a. The teachings of Ashkenazi *et al* as evidenced by InVitrogen Manual, Delgi-Esposti *et al* have been previously set forth in the previous office actions. Ashkenazi *et al* and Delgi-Esposti *et al* do not specifically teach a composition in which the fusion protein further comprises a growth media. Moreover, the references also fail to specifically teach the production of a composition at a reduced temperature. These deficiencies are remedied by Kaufmann *et al*.
- b. Kaufmann *et al* teach the use of a model system in which CHO cells are used to express a SEAP protein cultured at a reduced temperature of 30 degrees Celcius.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the SEAP protein of Kaufmann *et al* with the fusion proteins as provided by either Ashkenazi *et al* or Delgi-Esposti *et al*, because the prior art provides sufficient motivation to reduce the normal culturing temperature of mammalian cells such as CHO cells to a lower temperature such that there is an increased production of proteins. Kaufmann *et al* teach that in addition to the increasing

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the specific production of recombinant protein, it allows for longer culturing time in batch cultures and provides greater concentration of the recombinant protein (see page 580, for example). Thus one of skill in the art could easily substitute the SEAP protein of Kaufmann *et al* for the LTbR-Fc-Ig protein or HVEM-Ig-Fc protein as provided by Ashkenazi *et al* and Delgi-Esposti *et al*, respectively, to produce high yield and active protein as claimed. Those of skill in the art would have reasonable expectation of success in making this substitution, because methods of culturing at reduced temperatures for the higher production of recombinant protein is a well known and practiced method in the recombinant protein arts.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of


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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Christopher Yaen
Art Unit 1643
May 28 2007
PRIMARY EXAMINER